

Appl. No.: 10/762,078  
Amdt. dated 10/11/2007  
Reply to Office action of May 11, 2007

Amendments to the Claims:

1. (Canceled)
2. (Canceled)
3. (Canceled)
4. (Canceled)
5. (Canceled)
6. (Canceled)
7. (Canceled)
8. (Canceled)
9. (Currently amended) The ~~nucleotide affinity medium~~ alkyl-linked nucleotide non-homogeneous solid support of claim [[8]]32, wherein the solid support includes at least one member selected from the group consisting of an acrylamide, agarose, methacrylate, cellulose, nylon, silica, glass, ceramic, a magnetized particle, nitrocellulose, polystyrene, a thermoresponsive polymer, and derivatives thereof.
10. (Currently amended) The ~~nucleotide affinity medium~~ alkyl-linked nucleotide non-homogeneous solid support of claim [[9]]32, wherein the solid support is a beaded agarose.
11. (Canceled)

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12. (Canceled)

13. (Canceled)

14. (Canceled)

15. (Canceled)

16. (Canceled)

17. (Canceled)

18. (Canceled)

19. (Canceled)

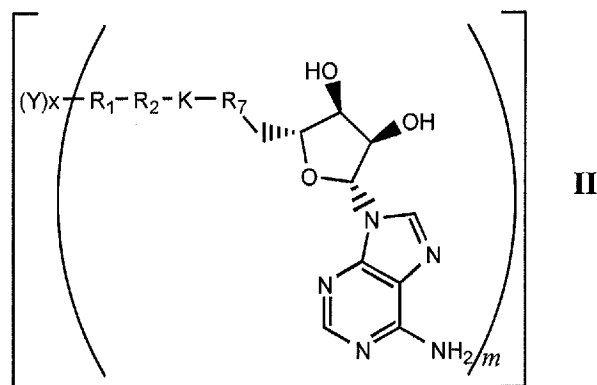
20. (Canceled)

21. (Canceled)

22. (Currently amended) The alkyl-linked nucleotide ~~composition~~ non-homogeneous solid support of claim ~~[[1]]~~ 32, wherein the ~~nucleoside~~ 5'-nucleosidyl group is selected from the group consisting of ~~[[an]]~~ a -5-deoxy-5'-adenosin[[e]]yl radical, a -5-deoxy-5'-guanosinyl radical, a -5-deoxy-5'-cytidin[[e]]yl radical, a -5-deoxy-5'-thymidin[[e]]yl radical, and ~~[[an]]~~ a -5-deoxy-5'-uridin[[e]]yl radical, or an analog thereof.

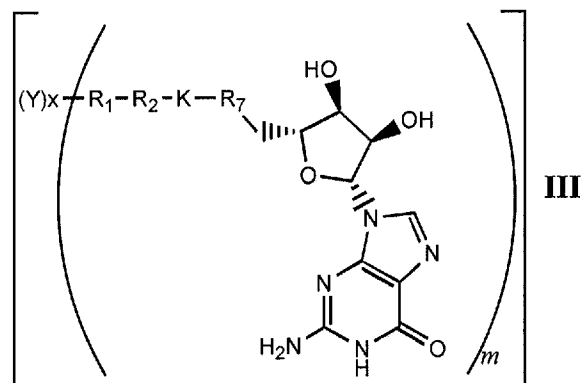
23. (Currently amended) The alkyl-linked nucleotide ~~composition~~ non-homogeneous solid support of claim 22, wherein the ~~nucleoside~~ 5'-nucleosidyl group is ~~[[an]]~~ a -5-deoxy-5'-

adenosin[[e]]yl radical, said alkyl-linked nucleotide ~~composition~~ non-homogeneous solid support consisting essentially of [[a]] the general structure:



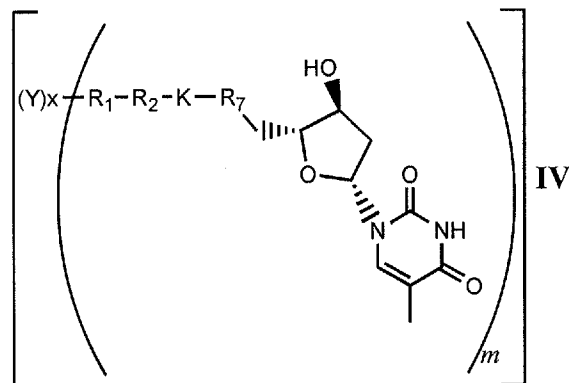
or an ionized variant or a salt thereof.

24. (Currently amended) The alkyl-linked nucleotide ~~composition~~ non-homogeneous solid support of claim 22, wherein the ~~nucleoside~~ 5'-nucleosidyl group is a -5-deoxy-5'-guanosinyl radical, said alkyl-linked nucleotide ~~composition~~ non-homogeneous solid support consisting essentially of [[a]] the general structure:



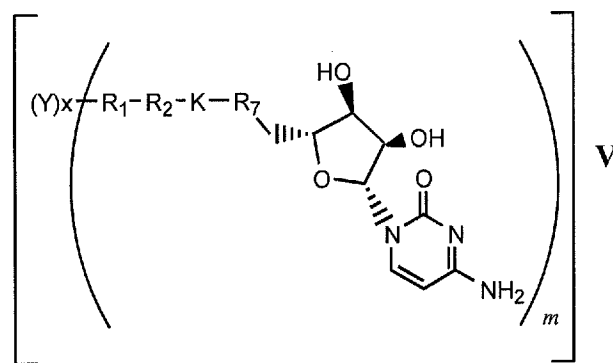
or an ionized variant or a salt thereof.

25. (Currently amended) The alkyl-linked nucleotide ~~composition~~ non-homogeneous solid support of claim 22, wherein the ~~nucleoside~~ 5'-nucleosidyl group is a -5-deoxy-5'-thymidin[[e]]yl radical, said alkyl-linked nucleotide ~~composition~~ non-homogeneous solid support consisting essentially of [[a]] the general structure:



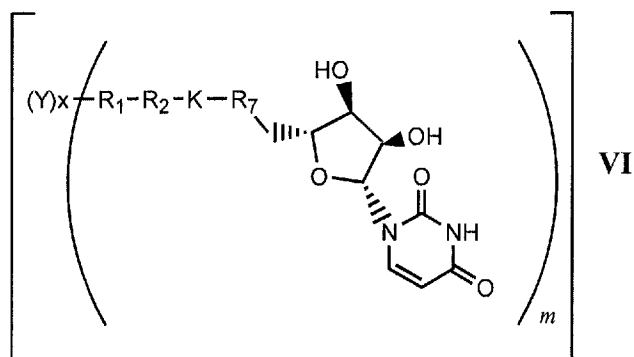
or an ionized variant or a salt thereof.

26. (Currently amended) The alkyl-linked nucleotide ~~composition~~ non-homogeneous solid support of claim 22, wherein the ~~nucleoside~~ 5'-nucleosidyl group is a -5-deoxy-5'-cytidin[[e]]yl radical, said alkyl-linked nucleotide ~~composition~~ non-homogeneous solid support consisting essentially of [[a]] the general structure:



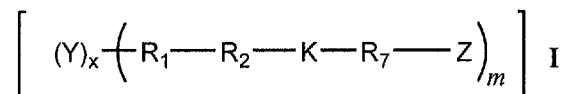
or an ionized variant or a salt thereof.

27. (Currently amended) The alkyl-linked nucleotide ~~composition~~ non-homogeneous solid support of claim 22, wherein the ~~nucleoside~~ 5'-nucleosidyl group is [[an]] a -5-deoxy-5'-uridin[[e]]yl radical, said alkyl-linked nucleotide ~~composition~~ non-homogeneous solid support consisting essentially of [[a]] the general structure:



or an ionized variant or a salt thereof.

28. (Currently amended) A method for synthesizing a nucleotide affinity medium consisting essentially of [[a]] the general formula:



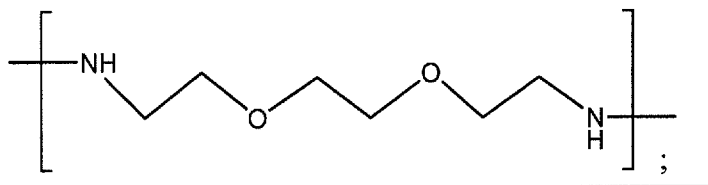
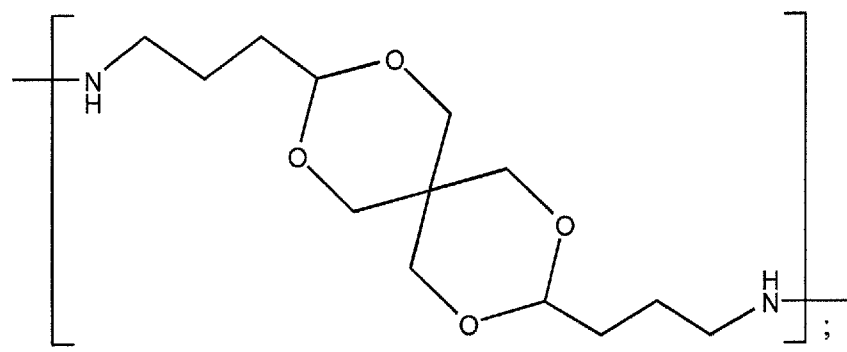
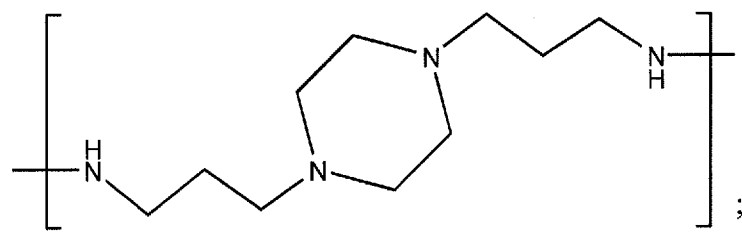
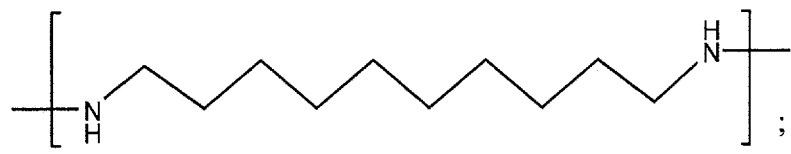
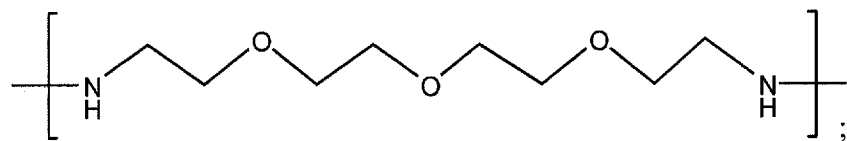
comprising the steps of:

- a) coupling at least one linker to a solid support in a suitable coupling buffer, wherein said linker is  $R_2$  or a combination of  $R_1$  and  $R_2$ ;
- b) end-capping at least a portion of reactive sites remaining on said solid support after said coupling step; and
- c) reacting a terminal phosphate or thiophosphate group of a nucleotide with said linker coupled to said solid support,

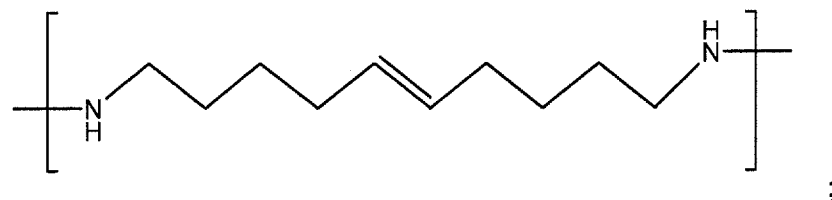
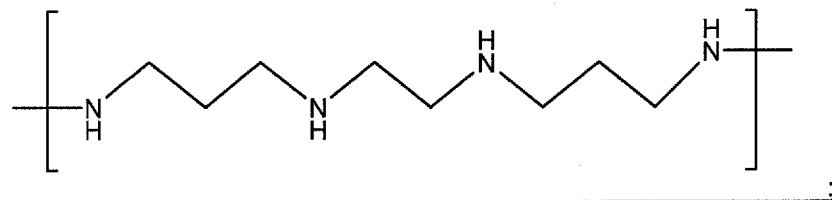
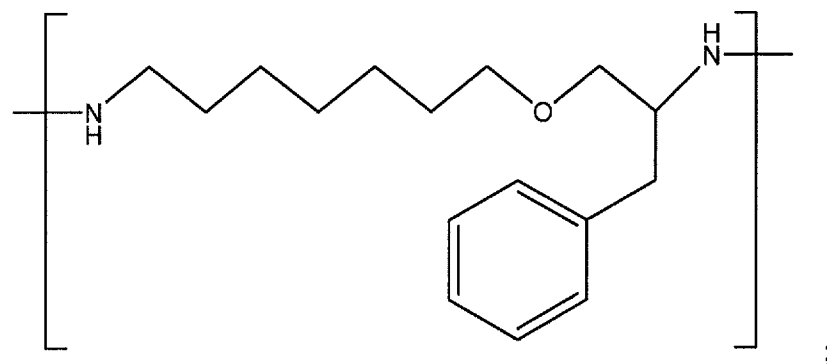
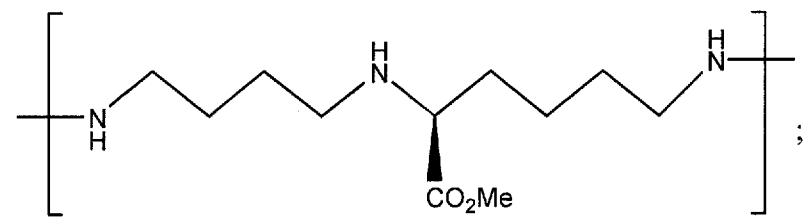
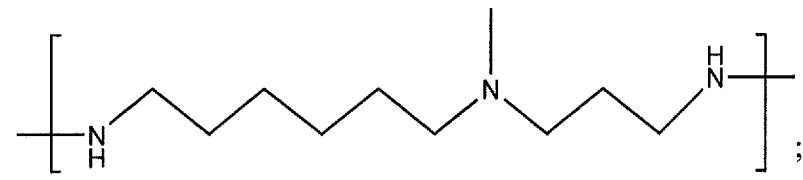
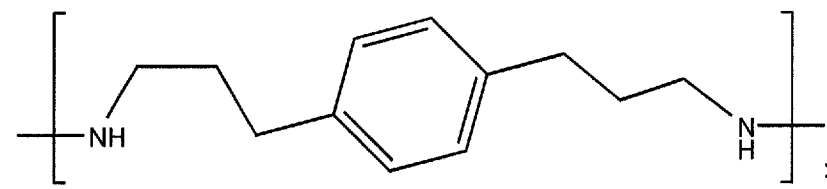
wherein Y is a solid support;  $x = 1$ ;  $R_1$  is a covalent bond between Y and  $R_2$ , or  $R_1$  is a divalent acyl group  $-C(=Q)-$ , wherein Q is O or  $NH_2^+[[,]]$  ~~a substituted or a non-substituted divalent alkyl group, a substituted or a non-substituted divalent cycloalkyl group, a substituted or a non-substituted divalent heteroalkyl group, a substituted or a non-substituted divalent heterocycloalkyl group, a substituted or a non-substituted divalent aryl group, a substituted or a non-substituted divalent heteroaryl group, or a combination thereof;~~  $R_2$  is a substituted or a non-substituted divalent alkyl group, a substituted or a non-substituted divalent cycloalkyl group, a substituted or a non-substituted divalent heteroalkyl group, a substituted or a non-substituted divalent heterocycloalkyl, a substituted or a non-substituted divalent heteroaryl group, or a

~~combination thereof~~; K is NH; R<sub>7</sub> is (P)<sub>n</sub> where P is a phosphate or thiophosphate and n is at least one ~~or R<sub>7</sub> is a phosphate group mimic~~; Z is a 5'-nucleosidyl group or a 5'-nucleosidyl group wherein the ~~nucleoside~~ 5'-nucleosidyl group is not naturally occurring, or a derivative thereof; and m is at least one;

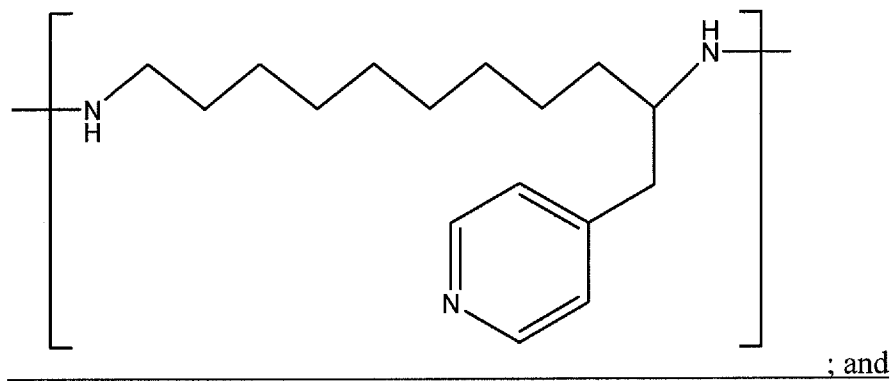
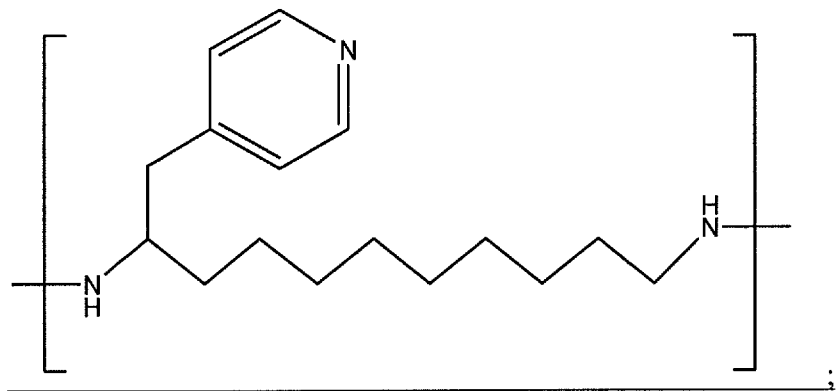
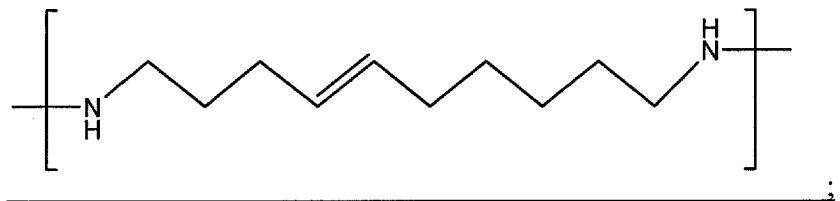
and -R<sub>2</sub>-K- is selected from the group consisting of:



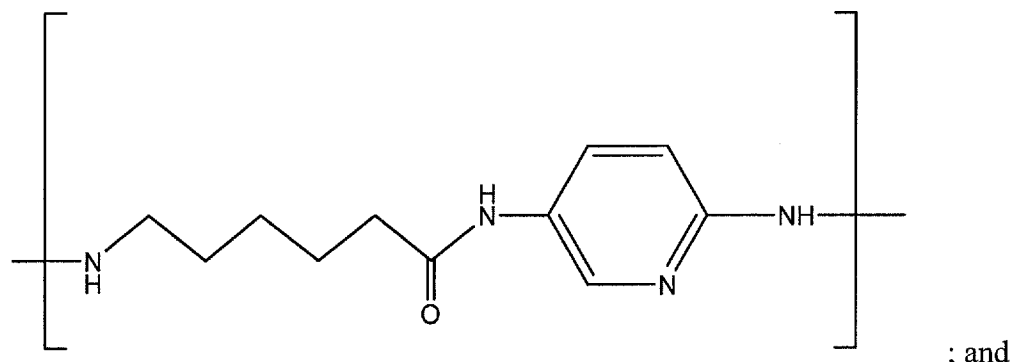
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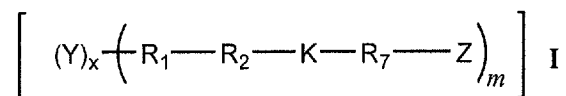
wherein the solid support has a loading of an alkyl-linked nucleotide having a range of about 20% to about 50%.

29. (Canceled)

30. (Canceled)

31. (Currently amended) A method for screening a test compound comprising the steps of:

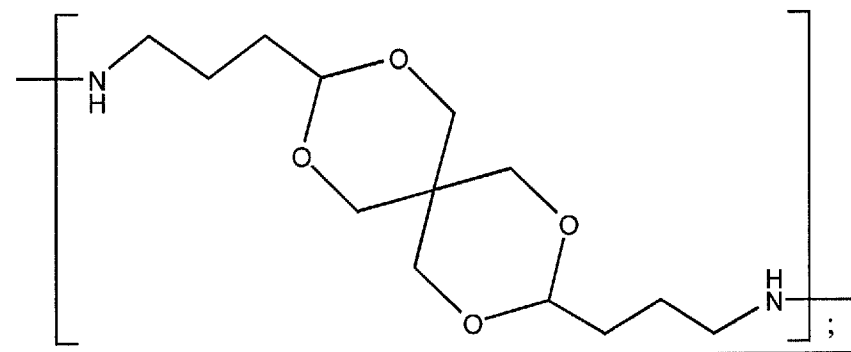
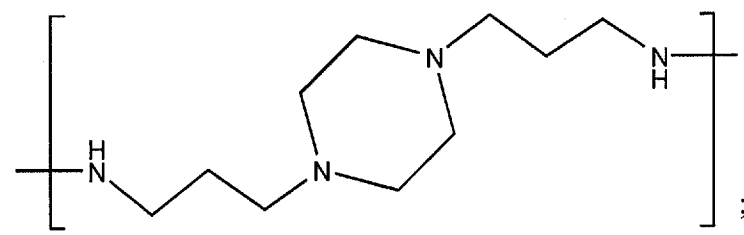
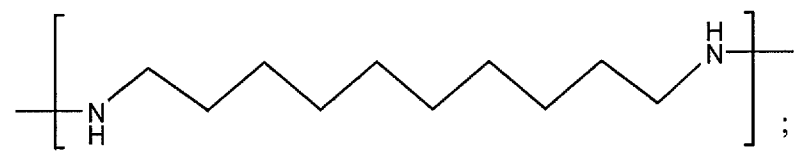
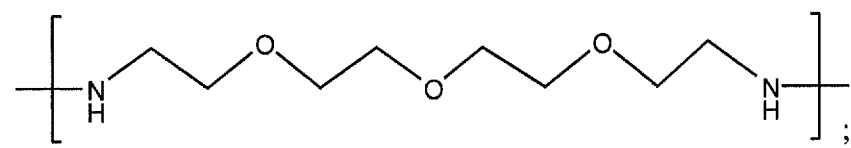
a) contacting a proteome with a nucleotide affinity medium consisting essentially of [[a]] the general formula:



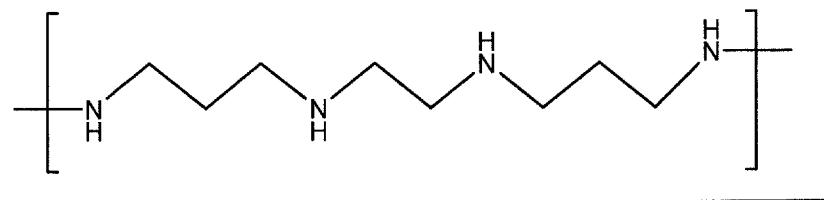
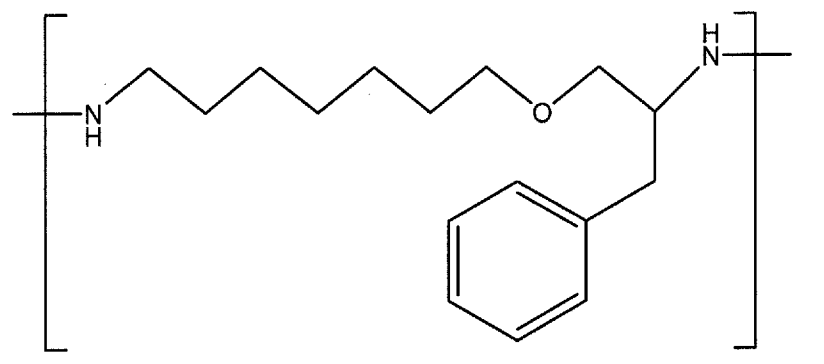
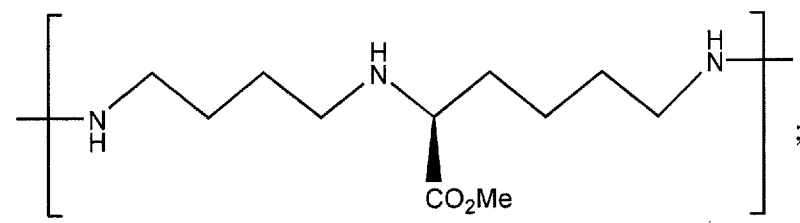
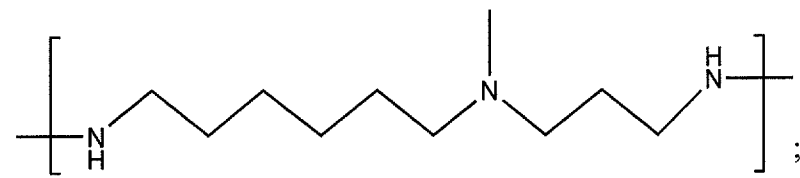
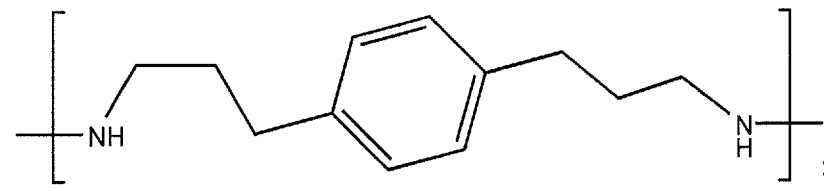
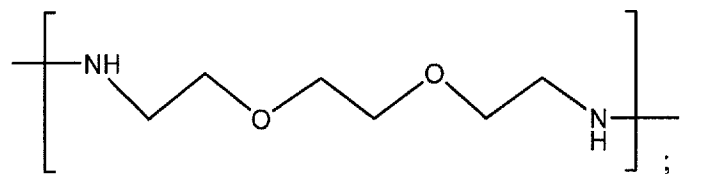
wherein Y is a solid support;  $x = 1$ ;  $R_1$  is a covalent bond between Y and  $R_2$ , or  $R_1$  is a divalent acyl group  $-C(=Q)-$ , wherein Q is O or  $NH_2^+$ , ~~a substituted or a non-substituted divalent alkyl group, a substituted or a non-substituted divalent cycloalkyl group, a substituted or a non-substituted divalent heteroalkyl group, a substituted or a non-substituted divalent heterocycloalkyl group, a substituted or a non-substituted divalent aryl group, a substituted or a non-substituted divalent heteroaryl group, or a combination thereof;~~  $R_2$  is a substituted or a non-substituted divalent alkyl group, a substituted or a non-substituted divalent cycloalkyl group, a substituted or a non-substituted divalent heteroalkyl group, a substituted or a non-substituted

~~divalent heterocycloalkyl, a substituted or a non-substituted divalent heteroaryl group, or a combination thereof;~~ K is NH; R<sub>7</sub> is (P)<sub>n</sub> where P is a phosphate or thiophosphate and n is at least one or ~~R<sub>7</sub> is a phosphate group mimic;~~ Z is a 5'-nucleosidyl group or a 5'-nucleosidyl group wherein the nucleoside is not naturally occurring, or a derivative thereof; and m is at least one[[]];

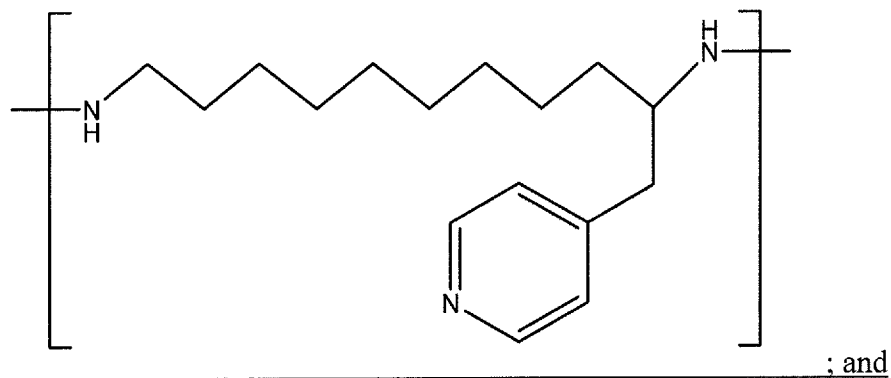
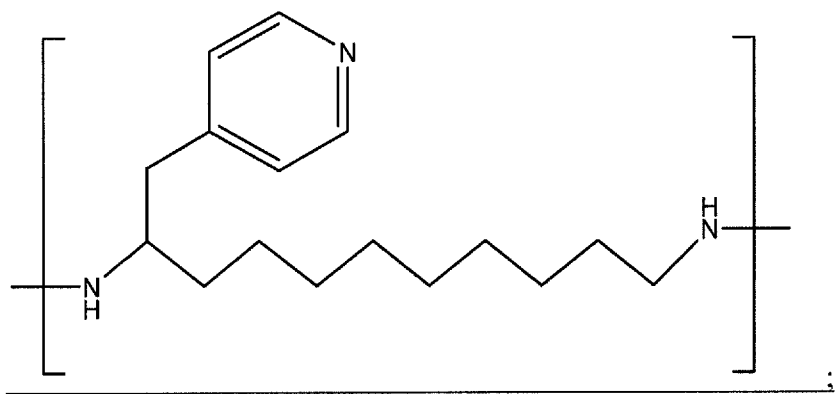
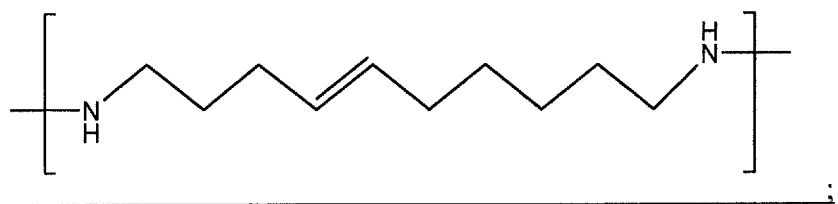
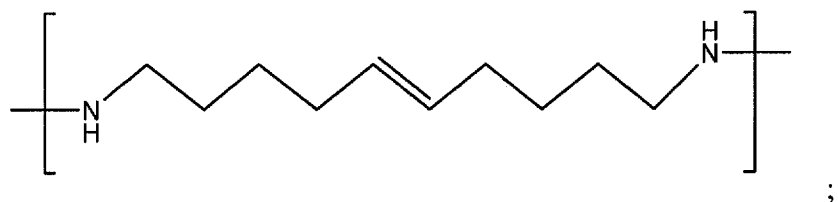
and -R<sub>2</sub>-K- is selected from the group consisting of:

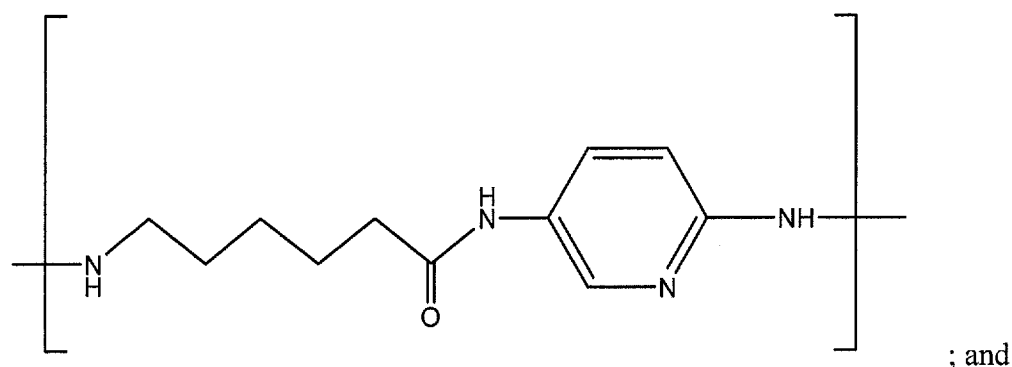


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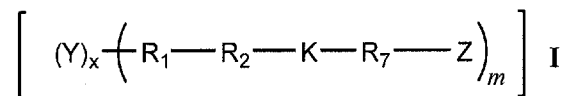




wherein the solid support has a loading of an alkyl-linked nucleotide having a range of about 20% to about 50%;

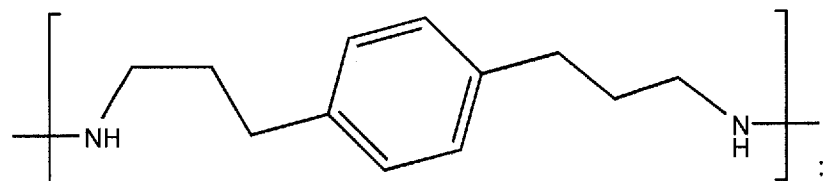
- b) washing the nucleotide affinity medium with a buffer, whereby non-specifically bound components of the proteome are eluted from the nucleotide affinity medium and specific components of the proteome remain bound to the nucleotide affinity medium;
- c) contacting the nucleotide affinity medium bound with specific components of the proteome with at least one test compound;
- d) eluting from the nucleotide affinity medium components of the proteome that are specifically displaced by the test compound; and
- e) identifying the components of the proteome that are specifically displaced by the test compound from the nucleotide affinity medium.

32. (New) An alkyl-linked nucleotide non-homogeneous solid support consisting essentially of the general formula:



wherein Y is a solid support;  $x = 1$ ;  $R_1$  is a covalent bond between Y and  $R_2$ , or  $R_1$  is a divalent acyl group  $-C(=Q)-$ , wherein Q is O or  $NH_2^+$ ; K is NH;  $R_7$  is  $(P)_n$  where P is a phosphate or a thiophosphate and n is at least one; and m is at least one; Z is a 5'-nucleosidyl group or a 5'-nucleosidyl group wherein the 5'-nucleosidyl group is not naturally occurring, or a derivative thereof; and  $-R_2-K-$  is selected from the group consisting of:

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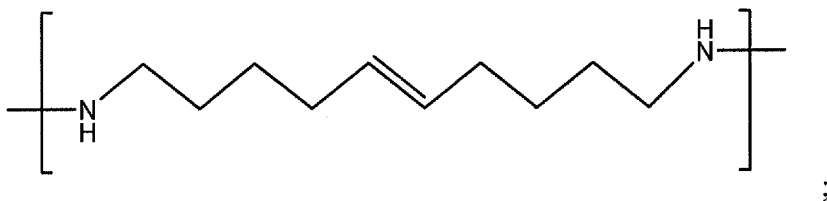
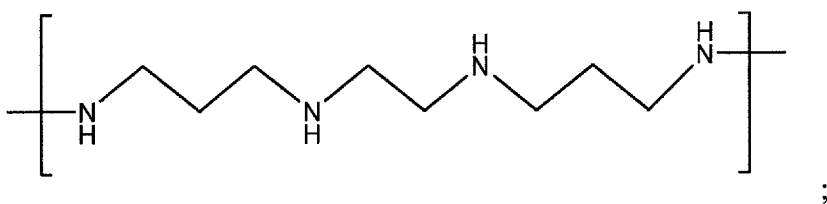
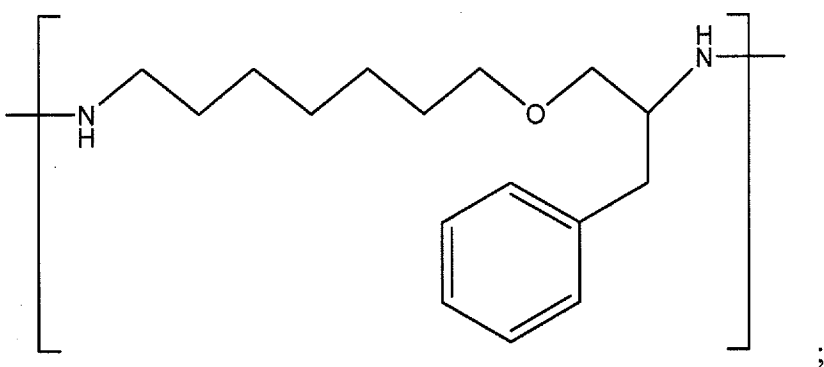
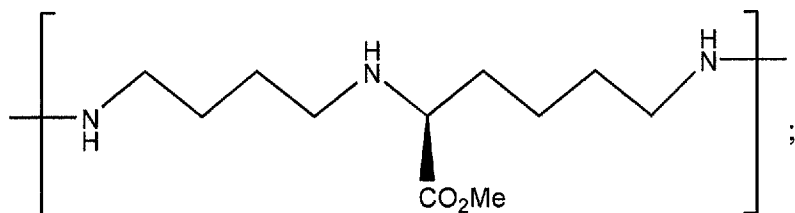
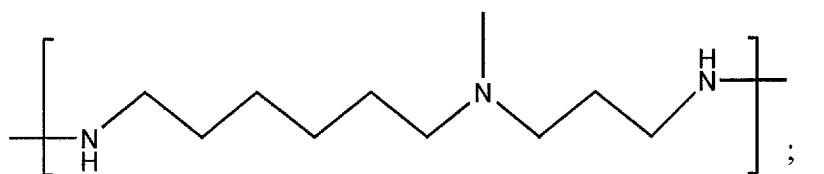


Figure 1: A diagram illustrating the relationship between the input variables  $x_1$  and  $x_2$  and the output variable  $y$ . The input variables are shown as nodes in a directed acyclic graph (DAG) that influence the output variable  $y$ . The graph shows a causal structure where  $x_1$  and  $x_2$  are parents of  $y$ , and there is a directed edge from  $x_1$  to  $x_2$ . The output variable  $y$  is shown as a node that is influenced by both  $x_1$  and  $x_2$ .





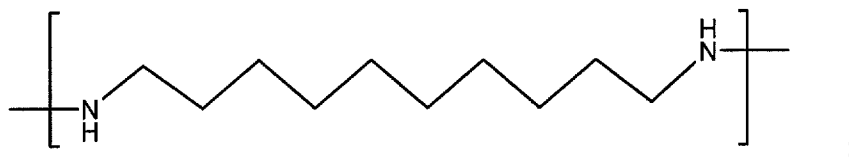
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wherein the solid support has a loading of an alkyl-linked nucleotide having a range of about 20% to about 50%.

33. (New) The alkyl-linked nucleotide non-homogeneous solid support of claim 32, wherein:

$R_1$  is  $-C(=NH_2^+)-$ ;

$R_2$  is:



P is phosphate; and

n is 3.